Rotavirus and Hepatitis A

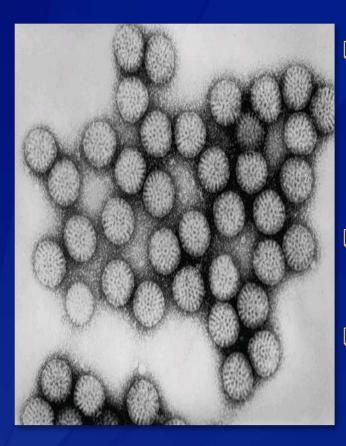
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Rotavirus

- First identified as a cause of diarrhea in 1973
- Most common cause of severe gastroenteritis in infants and young children
- Nearly universal infection by age 5
- Responsible for up to 500,000 diarrheal deaths each year worldwide

Rotavirus



- From 1996-2005, five predominate strains in the U.S. (G1-G4, G9) accounted for 90% of the isolates
- G1 strain accounts for 75% of infections
- Very stable and may remain viable for weeks or months if not disinfected

Rotavirus Pathogenesis

- Entry through the mouth
- Replication in the epithelium of the small intestine
- In severe infections rotavirus antigen detectable in serum
- Infection leads to isotonic diarrhea

Rotavirus Immunity

- Antibody against VP7 and VP4 probably important for protection
- First infection usually does not lead to permanent immunity
- Reinfection can occur at any age
- Subsequent infections generally less severe

Rotavirus – Clinical Features

- Short incubation period
- First infection after 3 months of age generally most severe
- May be asymptomatic or result is severe dehydrating diarrhea with fever and vomiting
- Gastrointestinal symptoms generally resolve in 3-7 days

Rotavirus Complications

- Severe diarrhea
- Dehydration
- Electrolyte imbalance
- Metabolic acidosis
- Immunodeficient children may have more severe or persistent disease

Rotavirus Epidemiology

- Reservoir
 - Human Gl tract and stool
- Transmission
 - Fecal-oral, fomites
- Temporal pattern
 - Fall and winter (temperate areas)
- Communicability
 - 2 days before to 10 days after onset of symptoms

Rotavirus Disease in the United States Prevaccine Era

- Annually responsible for:
 - 3 million infections
 - More than 400,000 physician visits
 - 200,000 emergency dept. visits
 - 55,000-70,000 hospitalizations
 - 20-60 deaths
- \$1 billion in direct and indirect costs





Notes from the Field: Outbreaks of Rotavirus Gastroenteritis Among Elderly Adults in Two Retirement Communities --- Illinois, 2011

Weekly

October 28, 2011 / 60(42);1456-1456

In February 2011, three residents of a retirement community in Illinois were hospitalized for acute gastroenteritis. The admitting physicians ordered testing of stool specimens for several pathogens, including rotavirus. The hospital laboratory detected rotavirus antigen in specimens from each patient, and the hospital infection control practitioner reported that information to the Cook County Department of Public Health. Two additional residents were hospitalized for rotavirus gastroenteritis shortly thereafter. The health department sent stool specimens from the five patients to CDC for testing for rotavirus and norovirus. Rotavirus was detected in each specimen; norovirus was not detected. During a subsequent investigation, all available residents were queried regarding recent diarrheal symptoms. Preliminary data indicated that 22% of residents had confirmed or probable rotavirus disease and 10 residents were hospitalized. In May 2011, another outbreak of rotavirus gastroenteritis was detected at a second retirement community in the county. On preliminary analysis, the overall attack rate in the second retirement community was 11%, and 20 residents were hospitalized. No deaths were identified in either outbreak. Based on preliminary results of the investigations and general knowledge of rotavirus transmission, within each community, rotavirus likely was transmitted from person to person via contaminated hands or fomites (e.g., environmental surfaces). The outbreaks lasted ≥4 weeks.

Rotavirus is well recognized as a major cause of severe gastroenteritis in young children. Rotavirus also can cause gastroenteritis in adults (1), but estimates of the disease burden are imprecise because rotavirus testing of adults rarely is performed. The extent to which rotavirus outbreaks occur

Rotavirus Vaccines

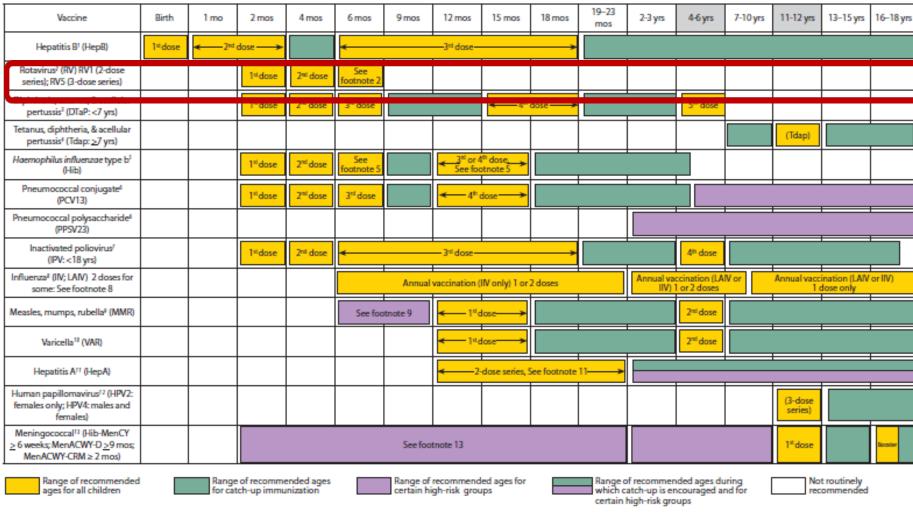
- RV5 (RotaTeq)
 - Contains five reassortant rotaviruses developed from human and bovine parent rotavirus strains
- RV1 (Rotarix)
 - Contains one strain of live attenuated human rotavirus (type G1PA[8])
- Both rotavirus vaccines
 - Are live, attenuated vaccine
 - Contain no preservatives or thimerosal

Rotavirus Vaccine Efficacy

- Any rotavirus gastroenteritis
 - **74%-87%**
- Severe gastroenteritis
 - **85%** 98%
- Both vaccines significantly reduced physician visits for diarrhea, and reduced rotavirus-related hospitalization
- No ACIP preference for one product (RV5 vs. RV1) over the other

Figure 1. Recommended immunization schedule for persons aged 0 through 18 years – United States, 2015. (FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE (FIGURE 21).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded.



This schedule includes recommendations in effect as of January 1, 2015. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm) or by telephone (800-CDC-INFO [800-232-4636]).

This schedule is approved by the Advisory Committee on Immunization Practices (http://www.aap.org), the American Academy of Pediatrics (http://www.aap.org), the American Academy of Family Physicians (http://www.aafp.org), and the American College of Obstetricians and Gynecologists (http://www.acog.org).

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Rotavirus Vaccination Schedule

Vaccine	Birth	1 mo	2 mos	4 mos	6 mas	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs
Rotavirus ² (RV) RV1 (2-dose series): RV5 (3-dose series)			1ªdose	2 nd dose	See footnote 2							

- Two RV1 or three RV5 oral doses beginning at 2 months of age
 - May be started as early as 6 weeks of age
- For both rotavirus vaccines
 - Maximum age for first dose is 14 weeks 6 days*
 - Minimum interval between doses is 4 weeks
 - Maximum age for any dose is 8 months 0 days

^{*}This is an off-label recommendation for both vaccines, because the labeled maximum age for the first dose of RV5 is 12 weeks

Rotavirus Vaccination Schedule

- ACIP did not define a maximum interval between doses
- No rotavirus vaccine should be administered to infants older than 8 months 0 days*
- It is not necessary to restart the series or add doses because of a prolonged interval between doses

^{*}This is an off-label recommendation for both vaccines, because the labeled maximum age for RV1 is 24 weeks, and the labeled maximum age for RV5 is 32 weeks

Rotavirus Vaccine Recommendations

- ACIP recommends that providers do not repeat the dose if the infant spits out or regurgitates the vaccine
- Any remaining doses should be administered on schedule
 - Doses of rotavirus vaccine should be separated by at least 4 weeks
- Complete the series with the same vaccine product whenever possible

Rotavirus Vaccine Recommendations

- If product used for a prior dose or doses is not available or not known, continue or complete the series with the product that is available
- If any dose in the series was RV5 (RotaTeq) or the vaccine brand used for any prior dose is not known, a total of 3 doses of rotavirus vaccine should be administered
- Infants documented to have had rotavirus gastroenteritis before receiving the full course of rotavirus vaccinations should still begin or complete the 2- or 3-dose schedule

Vaccine Administration

- Preparation:
 - RV5: None
 - RV1: Must be reconstituted BEFORE administering
- Route:
 - Both vaccines are administered ORALLY (PO)
- The infant may eat or drink immediately following vaccine administration
- RV vaccine may be administered simultaneously with other vaccines

Rotavirus Errors 2006-2013 VAERS

- Oral rotavirus vaccine injected* (39)
 - Rotarix (33), RotaTeq (6)
 - Adverse health events (19; 49%) irritability, injection site reactions
 - Reasons for error- misinterpreted instructions, confused Rotarix vial for injectable vaccine, inadequate training, not reading package insert
- Eye splashes* (27)
 - Eye splash following oral rotavirus vaccines with infant coughing, sneezing, or spitting the vaccine into eyes
 - Healthcare providers most commonly affected (80%)
 - Adverse health events in (21;78%) included eye irritation, hyperemia, pruritus, blurred vision
- Proper administration: Use the manufacturers' oral applicator devices (squirt gently and slowly into the child's cheek)

*Hibbs BF, Miller ER, Shimabukuro T. Centers for Disease Control and Prevention (CDC). Notes from the field: rotavirus vaccine administration errors-United States, 2006-2013. *MMWRMorb Mortal Wkly Rep.* 2014; 63(4):81

Rotavirus Vaccine Contraindications

- Severe allergic reaction to a vaccine component (including latex) or following a prior dose of vaccine
 - Latex rubber is contained in the RV1 oral applicator
- History of intussusception
- Severe combined immunodeficiency (SCID)

Rotavirus Vaccine Precautions*

- Altered immunocompetence, (except SCID, which is a contraindication)
 - Limited data do not indicate a different safety profile in HIV-infected versus HIV-uninfected infants
 - HIV diagnosis not established in infants due for rotavirus vaccine
 - Vaccine strains of rotavirus are attenuated
 - These considerations support rotavirus vaccination of HIV-exposed or infected infants
- Acute, moderate or severe gastroenteritis or other acute illness

^{*}The decision to vaccinate if a precaution is present should be made on a case-by-case risk and benefit basis

Rotavirus Vaccine – Conditions Not Considered to be Precautions

- Pre-existing chronic gastrointestinal conditions
 - No data available
 - ACIP considers the benefits of vaccination to outweigh the theoretic risks

Rotavirus and Preterm Infants

- ACIP supports vaccination of a preterm infant if:
 - Chronological age is at least 6 weeks
 - Clinically stable; and
 - Vaccine is administered at time of discharge or after discharge from neonatal intensive care unit or nursery

Household Contacts of Rotavirus Vaccine Recipients

- Infants living in households with persons who have or are suspected of having an immunodeficiency disorder or impaired immune status can be vaccinated
- Protection provided by vaccinating the infant outweighs the small risk of transmitting vaccine virus
- Infants living in households with pregnant women should be vaccinated
 - Majority of women of childbearing age have preexisting immunity to rotavirus
 - Risk for infection by vaccine virus is considered to be very low

Rotavirus Vaccine Adverse Events

- Intussusception
 - Postlicensure-evaluation RV1 1-3 excess cases per 100,000 first doses, possible risk for RV5 cases too small to confirm
 - VAERS reports show events cluster in 3-6 days following RV5
 - Vaccine Safety Datalink
 - No increased risk of intussusception unable to assess RV1

Rotavirus Vaccine Adverse Reactions

- □ RV5
 - Diarrhea 18.1%
 - Vomiting 11.6%
 - Also greater rates of otitis media, nasopharyngitis and bronchospasm
- □ RV1
 - Irritability 11.4%
 - Cough or runny nose 3.6%
 - Flatulence 2.2%

Vaccine Storage and Handling

- Store RV vaccines in the refrigerator between 35° - 46° F (2° - 8° C)
- Different lot numbers on the vaccine, the diluent, and the carton
- Lot number on the carton identifies the vaccine
- If space is limited to log lot numbers, document the lot number on the box





Rotavirus Resources

- ACIP's Rotavirus Recommendations web page
 - www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/rotavirus.html
- CDC's Rotavirus Infection web page www.cdc.gov/rotavirus/index.html
- □ CDC's Rotavirus Vaccination web page www.cdc.gov/vaccines/vpd-vac/rotavirus/default.htm
- Immunization Action Coalition Rotavirus web page www.immunize.org/rotavirus/
- Children's Hospital of Philadelphia Vaccine Education Center Rotavirus web page

www.chop.edu/service/vaccine-education-center/a-look-at-each-vaccine/rotavirus.html

HEPATITISA AND HEPATITISA VACCINES

Hepatitis A

- Epidemic jaundice described by Hippocrates
- Differentiated from Hepatitis B in 1940s
- Serologic tests developed in 1970s
- Vaccines licensed in 1995 and 1996

Hepatitis A Pathogenesis

- Entry into mouth
- Viral replication in the liver
- Virus present in the blood and feces
 10-12 days after infection
- Virus excretion may continue for up to 3 weeks after onset of symptoms

Hepatitis A Clinical Features

- Incubation period 28 days (range 15-50 days)
- Illness not specific for Hepatitis A
- Likelihood of symptomatic illness directly related to age
- Children generally asymptomatic, adults symptomatic

Hepatitis A Epidemiology

Reservoir Human

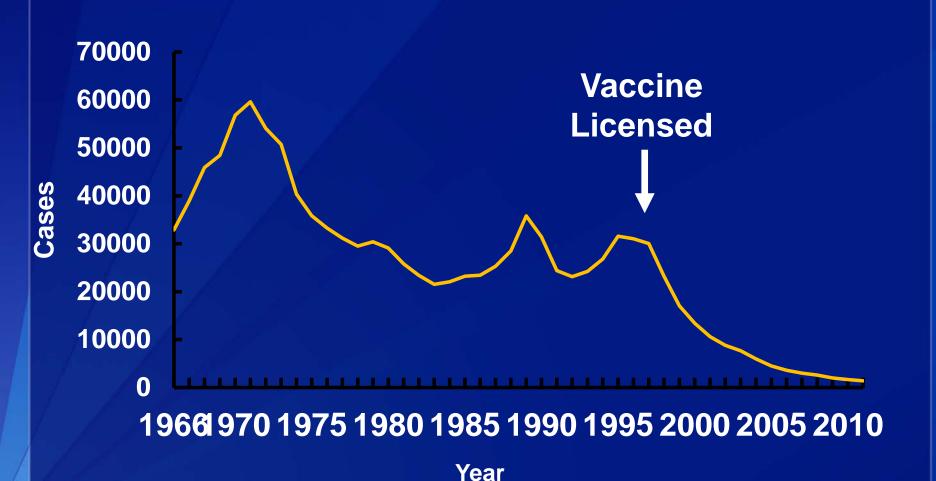
Transmission Fecal-oral

Temporal pattern None

Communicability

2 weeks before to 1 week after onset of jaundice

Hepatitis A - United States, 1966-2011



Hepatitis A Vaccines

- Inactivated vaccines
- Pediatric and adult formulations
 - Pediatric formulation of both vaccines is approved for children 1 through 18 years
 - Adult formulations approved for persons 19 years and older

Hepatitis A Vaccine Immunogenicity

Adults

- More than 95% seropositive after one dose
- Nearly 100% seropositive after two doses

Children and adolescents

- More than 97% seropositive after one dose
- 100% seropositive after 2 doses (in clinical trials)

Hepatitis A Vaccines

	HAVRIX VAQTA									
Pediatric Formulation										
Ages	1 through 18 years	1 through 18 years								
Dose/Volume	720 EL.U/0.5 mL	25 U/0.5 mL								
Adult Formulation										
Ages	19 years and older	19 years and older								
Dose/Volume	1,440 EL.U/1.0 mL	50 U/1.0 mL								
Both Formulations										
Number of Doses 2										
Schedule	0,6-12 months									
	(minimum interval = 6 months)									
Route	Intramuscular (IM) injection									

Hepatitis A Vaccine Efficacy

- □ HAVRIX (GSK)
 - 40,000 Thai children 1 to 16 years of age
 - Vaccine efficacy 94%
- VAQTA (Merck)
 - 1,000 New York children 2 to 16 years of age
 - Vaccine efficacy 100%

Twinrix

- Combination vaccine of:
 - Hepatitis A vaccine (pediatric dose)
 - Hepatitis B (adult dose)
- Schedules
 - 0, 1, 6 months, or
 - 0,7,21-30 days and booster dose at 12 months
- Approved for persons 18 years of age and older

Twinrix and Single Component Hepatitis A Vaccine

- Adult formulation hepatitis A vaccine may be used to complete a schedule begun with Twinrix and vice versa
- Acceptable schedules
 - 2 Twinrix and 1 Hepatitis A (adult formulation)
 - 1 Twinrix and 2 Hepatitis A (adult formulation)
- Maintain spacing recommended for Twinrix

^{*} For persons 19 years of age or older

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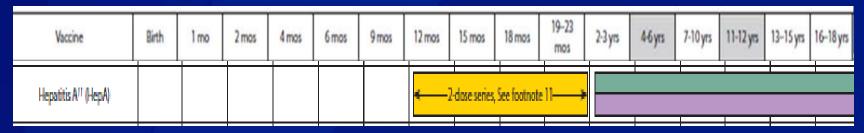
Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19–23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16-18 yrs
Hepatitis B ¹ (HepB)	1#dose	< 2 nd	dose		≪—3 rd dose——>											
Rotavirus ² (RV) RV1 (2-dose series); RV5 (3-dose series)			1#dose	2 rd dose	See footnote 2											
Diphtheria, tetanus, & acellular pertussis ¹ (DTaP: <7 yrs)			1 st dose	2 nd dose	3 rd dose			← 4 th	dose>			5 th dose				
Tetanus, diphtheria, & acellular pertussis¹ (Tdap: ≥7 yrs)														(Tdap)		
Haemophilus influenzae type b ⁵ (Hib)			1 st dose	2 nd dose	See footnote 5		3 rd or 4 See for	tnote 5								
Pneumococcal conjugate ⁶ (PCV13)			1 st dose	2 nd dose	3 rd dose		← 4 th	dose──➤								
Pneumococcal polysaccharide ⁶ (PPSV23)																
Inactivated poliovirus ⁷ (IPV: <18 yrs)			1#dose	2 nd dose	*		— 3 rd dose—		*			4 th dose				
Influenzal (IIV; LAIV) 2 doses for some: See footnote 8					Annual vaccination (IIV only) 1 or 2 doses						Annual vaccination (LAIV or IIV) 1 or 2 doses Annual vaccination (LAIV or IIV)					
Measles, mumps, rubella ^g (MMR)					See foo	tnote 9	← 1"c	iose >				2 nd dose				
Varicella [™] (VAR)							< 1 00	lose >				2 nd dose				
Hepatitis A ¹¹ (HepA)							< 2	dose series, S	see footnote	11>						
females only; HPV4: males and females)														(3-dose series)		
Meningococcal ¹³ (Hib-MenCY ≥ 6 weeks; MenACWY-D≥9 mos; MenACWY-CRM ≥ 2 mos)				See footnote 13										1 st dose		licater
Range of recommended ages Range of recommended ages Range of recommended ages for Range of recommended ages during Not routinely spes for all children which catch-up is encouraged and for recommended certain high-risk groups certain high-risk groups Range of recommended ages during Not routinely which catch-up is encouraged and for recommended certain high-risk groups Range of recommended ages during which catch-up is encouraged and for recommended recommended ages Range of recommended ages																

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NOTE: The above recommendations must be read along with the footnotes of this schedule.

Hepatitis A Vaccination of Children



- All children should receive vaccine at 12 through 23 months of age
- Vaccination should be integrated into the routine vaccination schedule
- Children who are not vaccinated by 2 years of age can be vaccinated at subsequent visits

ACIP Recommendations for Routine Hepatitis A Vaccination of Children (2)

- Existing Hepatitis A vaccination programs for children 2 through 18 years of age should be maintained
- New efforts on routine vaccination of children 12 months of age should enhance, not replace ongoing vaccination programs for older children
- In areas without an existing Hepatitis A vaccination program catch-up vaccination of unvaccinated children 2 through 18 years of age can be considered

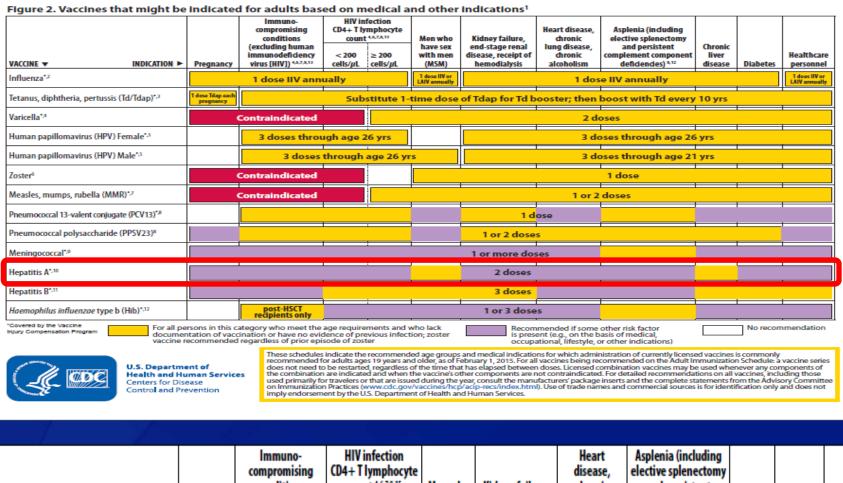
Recommended Adult Immunization Schedule—United States - 2015

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

Figure 1. Recommended adult immunization schedule, by vaccine and age group¹



^{*}Covered by the Vaccine Injury Compensation Program

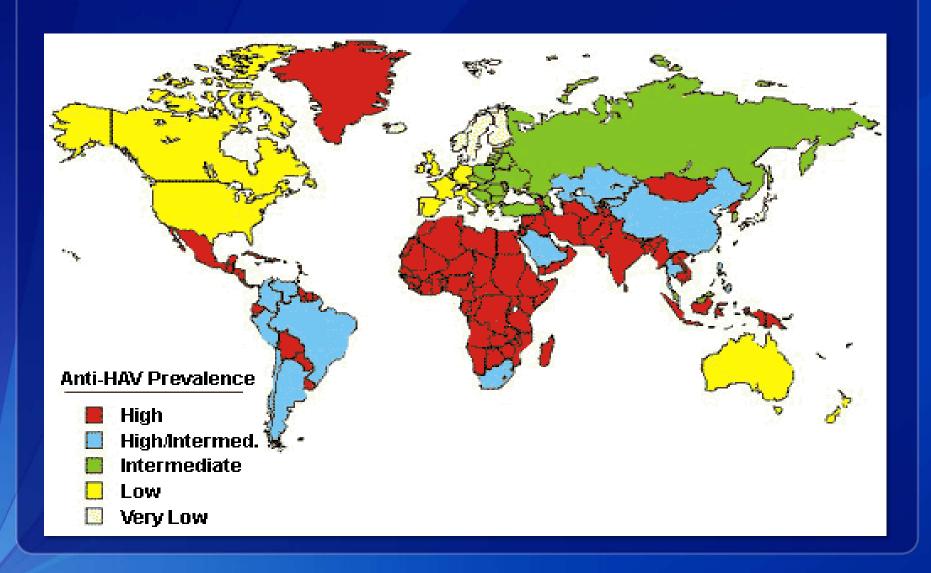


VA	CCINE ▼ INDICATION	► Pregnancy	Immuno- compromising conditions (excluding human immunodeficiency virus [HIV])4,6,7,8,15	<200 ≥200	Men who have sex	Kidney failure, end-stage renal disease, receipt of hemodialysis	chronic	Asplenia (including elective splenectomy and persistent complement component deficiencies) 8,14	Chronic liver	Diabetes	Healthcare personnel
He	patitis A ^{12,*}					2 doses					

Hepatitis A Immunization Recommendations for Adults

- International travelers
- Close contacts with an international adoptee from a country of high or intermediate endemicity
- Men who have sex with men
- Persons who use illegal drugs
- Persons who have a clotting-factor disorder
- Persons with occupational risk
- Persons with chronic liver disease, including Hepatitis C

Hepatitis A and International Travel



Hepatitis A for International Travelers

- The first dose of hepatitis A vaccine should be administered as soon as travel is considered
- For healthy persons 1 through 40 years of age:
 - 1 dose of single-component vaccine administered at any time before departure

Hepatitis A Vaccination for International Travelers (cont)

 Persons at risk of severe disease from Hepatitis A virus planning to travel in 2 weeks or sooner should receive the first dose of vaccine and also can be administered immune globulin

Vaccination for Close Contacts of Newly Arriving International Adoptees

- Hepatitis A vaccination for unvaccinated persons who anticipate close personal contact with an international adoptee from a country of high or intermediate endemicity during the first 60 days following arrival in the U.S.
- Administer dose 1 as soon as adoption is planned, ideally 2 or more weeks before the arrival of the adoptee

Hepatitis A Vaccination Recommendations for Adults (2)

- Men who have sex with men
- Persons who use illegal drugs
- Persons who have a clotting-factor disorder
- Persons with occupational risk
- Persons with chronic liver disease, including Hepatitis C

Hepatitis A Immunization Recommendations

- Not routinely recommended for:
 - Healthcare personnel
 - Child care center staff
 - Sewer workers or plumbers
- Food handlers: may be considered based on local circumstances

Hepatitis A Serologic Testing

- Prevaccination
 - Not indicated for children
 - May be considered for some adults and older adolescents
- Postvaccination
 - Not indicated

Hepatitis A Vaccine Contraindications and Precautions

- Severe allergic reaction to a vaccine component or following a prior dose
- Moderate or severe acute illness

Hepatitis A Vaccine Adverse Reactions

- Local reaction
- Systemic reactions (malaise, fatigue)
- No serious adverse reactions reported

20%-50%

Less than 10%

Vaccine Storage and Handling

 Store hepatitis A vaccine in a refrigerator between 35° - 46° F (2° - 8° C)

- Store pediatric and adult formulations
 - In their original packaging with the lids closed
 - In separate bins
 - Away from each other not next to each other





Hepatitis A Resources

- □ ACIP's Hepatitis A Recommendations web page www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/Hepatitis A.html
- CDC's Hepatitis A Infection web page www.cdc.gov/Hepatitis/HAV/index.htm
- □ CDC's Hepatitis A Vaccination web page www.cdc.gov/vaccines/vpd-vac/Hepatitis A/default.htm
- Immunization Action Coalition Hepatitis A web page

www.immunize.org/Hepatitis-a/

 Children's Hospital of Philadelphia Vaccine Education Center Hepatitis A web page

www.chop.edu/service/vaccine-education-center/a-look-at-each-vaccine/Hepatitis-a-vaccine.html